

FILE 'MEDLINE'
 FILE 'JAPIO'
 FILE 'BIOSIS'
 FILE 'SCISEARCH'
 FILE 'WPIDS'
 FILE 'CAPLUS'
 FILE 'EMBASE'
 => s g protein coupled receptor or gpcr
 5 FILES SEARCHED...

L1 39380 G PROTEIN COUPLED RECEPTOR OR GPCR

=> s 11 and (gpr38 or v279k)
 L2 28 L1 AND (GPR38 OR V279K)

=> dup rem l2

PROCESSING COMPLETED FOR L2

L3 8 DUP REM L2 (20 DUPLICATES REMOVED)

=> d l3 ibib abs 1-8

L3 ANSWER 1 OF 8 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 1

ACCESSION NUMBER: 2002-566812 [60] WPIDS

CROSS REFERENCE: 2002-508526 [54]; 2002-599814 [64]; 2002-643374 [69]

DOC. NO. NON-CPI: N2002-448649

DOC. NO. CPI: C2002-160764

TITLE: Assay for detecting Alzheimer's disease, Parkinson's disease, ulcerative colitis, Crohn's disease, Hodgkin's disease, glioblastoma or carcinoma, comprises using a binding partner for ***G*** ***protein*** ***coupled*** ***receptor*** 38.

DERWENT CLASS: B04 D16 J04 S03

INVENTOR(S): BROWN, J P; BURMER, G C; KULANDER, B G; ROUSH, C L

PATENT ASSIGNEE(S): (LIFE-N) LIFESPAN BIOSCIENCES INC

COUNTRY COUNT: 98

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2002057791 A2 20020725 (200260)* EN 112

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZM ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
 RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002057791 A2		WO 2001-US45219	20011129

PRIORITY APPLN. INFO: US 2000-250452P 20001130; US 2000-250251P
 20001129

AN 2002-566812 [60] WPIDS

CR 2002-508526 [54]; 2002-599814 [64]; 2002-643374 [69]

AB WO 200257791 A UPAB: 20021031

NOVELTY - An assay (M1) comprising contacting a binding partner specific for ***G*** ***protein*** ***coupled*** ***receptor*** (GPR) 38 with specific cells, is new.

DETAILED DESCRIPTION - (M1) comprises:

(a) providing a binding partner specific for GPR 38;
 (b) contacting the binding partner with neurons and astrocytes of the patient to allow the binding partner to bind ***GPR38*** in the cells;
 (c) detecting the binding partner bound to the GPR 38; and
 (d) determining whether one of the cells contains reduced levels of GPR 38 relative to normal.

INDEPENDENT CLAIMS are also included for:

(1) an assay (M2) for Parkinson's disease using (M1), where the binding partner is contacted with neurons and neuropil;

(2) an assay (M3) for ulcerative colitis using (M1), where the binding partner is contacted with surface epithelium neuroendocrine

cells, enteric plexus ganglion cells, subsets of lymphoid cells, and subsets of fibroblasts from a colon of the patient and determining whether the cells contain increased levels of GPR 38;

(3) an assay (M4) for Crohn's disease using (M1), where the binding partner is contacted with absorptive epithelium, neuroendocrine cells, or eosinophils from a small intestine of the patient;

(4) an assay (M5) for glioblastoma using (M1), where the binding partner is contacted with neoplastic glial cells to allow binding the glial cells or lymphoid cells;

(5) an assay (M6) for Hodgkin's disease using (M1), where the binding partner is contacted with Reed Sternberg cells and reactive lymphoid cells and determining whether the Reed Sternberg cells contain increased levels of GPR 38 and the reactive lymphoid cells contain focal punctuate staining of GPR 38;

(6) an assay (M7) for any carcinoma using (M1), where the binding partner is contacted with breast, colon, lung, ovarian, pancreas, or prostate tissue;

(7) a kit for the detection of antibodies against GPR 38 for use in (M1) comprising:

(a) an antibody specific for GPR 38;

(b) one or both of a reagent or a device for detecting the antibody;

and

(c) a label stating that the kit is to be used in the assay; and

(8) manufacturing a medicament able to reduce symptoms associated with Alzheimer's disease, Parkinson's disease, ulcerative colitis, Crohn's disease, Hodgkin's disease, glioblastoma, breast carcinoma, colon carcinoma, lung small cell carcinoma, lung adenocarcinoma, pancreatic small cell carcinoma and pancreatic adenocarcinoma comprising using a GPR 38 agonist or antagonist.

ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Antiulcer; Antiinflammatory; Cytostatic.

No suitable data given.

MECHANISM OF ACTION - GPR 38 agonist; ***GPR38*** antagonist; Gene therapy.

USE - (M1) is useful for the detection of an increased risk of Alzheimer's disease, Parkinson's disease, ulcerative colitis, Crohn's disease, Hodgkin's disease, glioblastoma, or carcinoma. GPR 38 is used to manufacture a medicament for inhibiting, treating or preventing Alzheimer's disease, Parkinson's disease, ulcerative colitis, Crohn's disease, Hodgkin's disease, glioblastoma, breast carcinoma, colon carcinoma, lung small cell carcinoma, lung adenocarcinoma, pancreatic small cell carcinoma, and pancreatic adenocarcinoma. An agonist or antagonist to GPR 38 are used to manufacture a medicament able to reduce the symptoms of these diseases (all claimed). Nucleic acids encoding GPR 38 can also be used to treat the diseases.

Dwg.0/1

L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:396891 CAPLUS

DOCUMENT NUMBER: 135:14332

TITLE: Method of forming a peptide-receptor complex with protein zsig33 and growth hormone secretagogue receptor (GHS-R)

INVENTOR(S): Sheppard, Paul O.; Jaspers, Stephen R.; Deisher, Theresa A.; Bishop, Paul D.

PATENT ASSIGNEE(S): ZymoGenetics, Inc., USA

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038355	A2	20010531	WO 2000-US32074	20001122
WO 2001038355	A3	20011122		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

EP 1232175 A2 20020821 EP 2000-982197 20001122

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:

US 1999-166765P P 19991122
WO 2000-US32074 W 20001122

AB The present invention relates to a method of forming a peptide-receptor complex with zsig33 polypeptides and growth hormone secretagogue receptor (GHS-R). The discovery of this novel method of forming a peptide-receptor complex is important for further elucidation of the how the body maintains its nutritional homeostasis and development of therapeutics to intervene in those processes, as well as other uses that will be apparent from the teachings herein. The present invention is based upon the identification of a previously described secreted protein known as zsig33 as the peptide ligand for an orphan receptor known as GHS-R, which belongs to ***G*** - ***protein*** - ***coupled*** - ***receptor*** family. The zsig33 ligand has homol. to motilin and has been found to be transcribed in the gastrointestinal system. The orphan receptor has homol. to the motilin receptor, ***GPR38***. Anal. of the tissue distribution of the mRNA corresponding to zsig33 protein showed that expression was highest in stomach, followed by apparent but decreased expression levels in small intestine and pancreas. The partial sequence for the secreted zsig33 protein was derived from a pancreatic library, and has also been shown in lung cDNA libraries. In vitro binding studies have shown that the zsig33 peptide binds to kidney, duodenum, and jejunum. Thus, binding of the zsig33 ligand to the GHS-R is expected in tissues such as stomach, small intestine, pancreas, lung, kidney, duodenum, jejunum, and brain. Methods of modulating gastric contractility, nutrient uptake, growth hormones, the secretion of digestive enzymes and hormones, and/or secretion of enzymes and/or hormones in the pancreas are also included.

L3 ANSWER 3 OF 8

MEDLINE

DUPLICATE 2

ACCESSION NUMBER: 2001230096 MEDLINE

DOCUMENT NUMBER: 21219832 PubMed ID: 11322507

TITLE: Growth hormone secretagogue receptor family members and ligands.

AUTHOR: Smith R G; Leonard R; Bailey A R; Palyha O; Feighner S; Tan C; McKee K K; Pong S S; Griffin P; Howard A

CORPORATE SOURCE: Huffington Center on Aging and Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX 77030-3498, USA.. rsmith@bcm.tmc.edu

SOURCE: ENDOCRINE, (2001 Feb) 14 (1) 9-14. Ref: 40
Journal code: 9434444. ISSN: 0969-711X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200108

ENTRY DATE: Entered STN: 20010827

Last Updated on STN: 20010827

Entered Medline: 20010823

AB We have previously reported the cloning and characterization of a new orphan ***G*** - ***protein*** - ***coupled*** - ***receptor*** (GPC-R), the growth hormone secretagogue receptor (GHS-R), and shown that this receptor mediates the activity of the growth hormone-releasing peptides (GHRPs) and nonpeptide ligands such as L-692,429 and MK-0677. Because the GHS-R obviously does not belong to any of the known GPC-R subfamilies, we searched for GHS-R family members by screening a human genomic library using low-stringency hybridization and screening a Pufferfish genomic library. The Pufferfish was selected because of its compact genome. From the human genomic library, a homolog, ***GPR38***, with 52% identity to the GHS-R was isolated. From the Pufferfish library, three family members were isolated. The Pufferfish gene having 58% identity to the GHS-R, on expression in HEK293 cells, was activated with GHRP-6 and MK-0677. These results indicate that the GHS-R has been conserved for at least 400 million years and that the Pufferfish genome is appropriate for isolation of GHS-R family members. In our search for endogenous ligands for the orphan receptors GHS-R and ***GPR38***, we showed that adenosine is a partial agonist of the GHS-R and that motilin is the endogenous ligand for ***GPR38***. We also confirmed that the endogenous ligand ghrelin is a full agonist of the GHS-R.

L3 ANSWER 4 OF 8

MEDLINE

DUPLICATE 3

ACCESSION NUMBER: 2000092336 MEDLINE

DOCUMENT NUMBER: 20092336 PubMed ID: 10628755

TITLE: Ligand activation domain of human orphan growth hormone

(GH) secretagogue receptor (GHS-R) conserved from

AUTHOR: Pufferfish to humans.
Palyha O C; Feighner S D; Tan C P; McKee [REDACTED]; Hreniuk D L;
Gao Y D; Schleim K D; Yang L; Morriello G J; Nargund R;
Patchett A A; Howard A D; Smith R G

CORPORATE SOURCE: Department of Biochemistry and Physiology, Merck Research
Laboratories, Rahway, New Jersey 07065, USA.

SOURCE: MOLECULAR ENDOCRINOLOGY, (2000 Jan) 14 (1) 160-9.
Journal code: 8801431. ISSN: 0888-8809.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200001

ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

AB Synthetic ligands have been identified that reset and amplify the cycle of pulsatile GH secretion by interacting with the orphan GH-secretagogue receptor (GHS-R). The GHS-R is rhodopsin like, but does not obviously belong to any of the established ***G*** ***protein*** - ***coupled*** ***receptor*** (***GPCR***) subfamilies. We recently characterized the closely related orphan family member, ***GPR38***, as the motilin receptor. A common property of both receptors is that they amplify and sustain pulsatile biological responses in the continued presence of their respective ligands. To efficiently identify additional members of this new ***GPCR*** family, we explored a vertebrate species having a compact genome, that was evolutionary distant from human, but where functionally important genes were likely to be conserved. Accordingly, three distinct full-length clones, encoding proteins of significant identity to the human GHS-R, were isolated from the Pufferfish (*Spherooides nephelus*). Southern analyses showed that the three cloned Pufferfish genes are highly conserved across species. The gene with closest identity (58%) was activated by three synthetic ligands that were chosen for their very high selectivity on the GHS-R as illustrated by their specificity in activating the wild-type human GHS-R but not the E124Q mutant. These results indicate that the ligand activation domain of the GHS-R has been evolutionary conserved from Pufferfish to human (400 million years), supporting the notion that the GHS-R and its natural ligand play a fundamentally important role in biology. Furthermore, they illustrate the power of exploiting the compact Pufferfish genome for simplifying the isolation of endocrinologically important receptor families.

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:426503 CAPLUS
DOCUMENT NUMBER: 131:194440
TITLE: Receptor for motilin identified in the human
gastrointestinal system
AUTHOR(S): Feighner, Scott D.; Tan, Carina P.; McKee, Karen
Kulju; Palyha, Oksana C.; Hreniuk, Donna L.; Pong,
Sheng-Shung; Austin, Christopher P.; Figueroa, David;
MacNeil, Douglas; Cascieri, Margaret A.; Nargund,
Ravi; Bakshi, Raman; Abramovitz, Mark; Stocco, Rino;
Kargman, Stacia; O'Neill, Gary; Van Der Ploeg, Lex H.
T.; Evans, Jilly; Patchett, Arthur A.; Smith, Roy G.;
Howard, Andrew D.

CORPORATE SOURCE: Department of Metabolic Disorders, Department of
Medicinal Chemistry, Merck Research Laboratories,
Rahway, NJ, 07065, USA

SOURCE: Science (Washington, D. C.) (1999), 284(5423),
2184-2188

PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Motilin is a 22-amino acid peptide hormone expressed throughout the
gastrointestinal (GI) tract of humans and other species. It affects
gastric motility by stimulating interdigestive antrum and duodenal
contractions. A heterotrimeric guanosine triphosphate-binding protein (***G*** ***protein***)- ***coupled*** ***receptor*** for
motilin was isolated from human stomach, and its amino acid sequence was
found to be 52 percent identical to the human receptor for growth hormone
secretagogues. The macrolide antibiotic erythromycin also interacted with
the cloned motilin receptor, providing a mol. basis for its effects on the
human gastrointestinal tract. The motilin receptor is expressed in
enteric neurons of the human duodenum and colon. Development of motilin
receptor agonists and antagonists may be useful in the treatment of

multiple disorders of gastrointestinal motility.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 8 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000062727 MEDLINE
DOCUMENT NUMBER: 20062727 PubMed ID: 10592437
TITLE: Growth hormone releasing substances: types and their receptors.
AUTHOR: Smith R G; Palyha O C; Feighner S D; Tan C P; McKee K K;
Hreniuk D L; Yang L; Morriello G; Nargund R; Patchett A A;
Howard A D
CORPORATE SOURCE: Huffington Center on Aging and Department of Cell Biology,
Baylor College of Medicine, Houston, TX 77030-3498, USA.
rsmith@bcm.tmc.edu
SOURCE: HORMONE RESEARCH, (1999) 51 Suppl 3 1-8. Ref: 55
Journal code: 0366126. ISSN: 0301-0163.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000411

AB A series of structurally diverse growth hormone (GH) releasing substances have been synthesized that are distinct from the naturally occurring GH releasing hormone (GHRH). These synthetic molecules range from the family of GH releasing peptides and mimetics such as MK-0677. The physiological importance of these molecules and their receptor is exemplified by studies in the elderly. For example, when MK-0677 was administered chronically to 70- to 90-year-old subjects, once daily, the age-related reduced amplitude of GH pulses was reversed to that of the physiological profile typical of young adults. In 1996, the synthesis of (35)S-MK-0677 was reported and used as a ligand to characterize a common receptor (GH secretagogue receptor [GHS-R]) for the GH releasing substances. The GHS-R is distinct from the GHRH receptor. Subsequently, the GHS-R gene was cloned and shown to encode a unique ***G*** - ***protein*** - ***coupled***

receptor with a deduced protein sequence that was 96% identical in human and rat. Because of the physiological importance of the GHS-R, a search for family members (FMs) was initiated and its molecular evolution investigated. Three FMs ***GPR38***, GPR39 and FM3 were isolated from human genomic libraries. To accelerate the identification of other FMs, a vertebrate organism with a compact genome distant in evolutionary terms from humans was exploited. The pufferfish (*Spherooides nephelus*) genome provides an ideal model for the discovery of human genes. Three distinct full-length clones encoding proteins of significant sequence identity to the human GHS-R were cloned from the pufferfish. Remarkably, the pufferfish gene with highest sequence homology to the human receptor was activated by the hexapeptide and non-peptide ligands. These intriguing results show that the structure and function of the ligand binding pocket of the human GHS-R has been highly conserved in evolution (approximately 400 million years) and strongly suggests that an endogenous natural ligand has been conserved. This new information is consistent with a natural ligand for the GHS-R playing a fundamentally important and conserved role in physiology. Copyright Copyright 1999 S. Karger AG, Basel

L3 ANSWER 7 OF 8 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999000845 MEDLINE
DOCUMENT NUMBER: 99000845 PubMed ID: 9782091
TITLE: Cloning and characterization of a human and murine T-cell orphan ***G*** - ***protein*** - ***coupled***
receptor similar to the growth hormone secretagogue and neurotensin receptors.
AUTHOR: Tan C P; McKee K K; Liu Q; Palyha O C; Feighner S D;
Hreniuk D L; Smith R G; Howard A D
CORPORATE SOURCE: Department of Biochemistry and Physiology, Merck Research Laboratories, Building RY-80Y-265, Rahway, New Jersey, 07065, USA.
SOURCE: GENOMICS, (1998 Sep 1) 52 (2) 223-9.
Journal code: 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-AF044600; GENBANK-AF044601
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19981207

AB Growth hormone secretagogues (GHS) are a group of synthetic peptide and nonpeptide molecules that potently stimulate the release of GH from the anterior pituitary gland through the activation of a novel ***G*** - ***protein*** - ***coupled*** ***receptor*** (GPC-R), the GHS-R. In our search for GHS-R family members, we recently described the cloning of two related GPC-Rs, ***GPR38*** and 39. In the present report, we detail the isolation of a new GPC-R (FM-3) from human and mouse with moderate sequence identity to both the GHS-R and neuropeptidyl-R. FM-3 is expressed in a diverse set of tissues.
Copyright 1998 Academic Press.

L3 ANSWER 8 OF 8 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1998110578 MEDLINE
DOCUMENT NUMBER: 98110578 PubMed ID: 9441746
TITLE: Cloning and characterization of two human ***G***
protein - ***coupled*** ***receptor*** genes
(***GPR38*** and GPR39) related to the growth hormone
secretagogue and neuropeptidyl receptors.
AUTHOR: McKee K K; Tan C P; Palyha O C; Liu J; Feighner S D;
Hreniuk D L; Smith R G; Howard A D; Van der Ploeg L H
CORPORATE SOURCE: Department of Biochemistry and Physiology, Merck Research
Laboratories, Rahway, New Jersey 07065, USA.
SOURCE: GENOMICS, (1997 Dec 15) 46 (3) 426-34.
Journal code: 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF034632; GENBANK-AF034633
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980319
Last Updated on STN: 20000303
Entered Medline: 19980309

AB The recent cloning of a growth hormone secretagogue receptor (GHS-R) from human pituitary gland and brain identified a third ***G***
protein - ***coupled*** ***receptor*** (GPC-R) involved in the control of growth hormone release. The nucleotide sequence of the GHS-R is most closely related to the neuropeptidyl receptor-1 (NT-R1) (35% overall protein identity). Two human GPC-Rs related to both the type 1a GHS-R and NT-Rs were cloned and characterized. Hybridization at low posthybridizational stringency with restriction enzyme-digested human genomic DNA resulted in the identification of a genomic clone encoding a first GHS-R/NT-R family member (***GPR38***). A cDNA clone was identified encoding a second GHS-R-related gene (GPR39). ***GPR38*** and GPR39 share significant amino acid sequence identity with the GHS-R and NT-Rs 1 and 2. An acidic residue (E124) in TM-3, essential for the binding and activation of the GHS-R by structurally dissimilar GHSSs, was conserved in ***GPR38*** and GPR39. ***GPR38*** is encoded by a single gene expressed in thyroid gland, stomach, and bone marrow. GPR39 is encoded by a highly conserved single-copy gene, expressed in brain and other peripheral tissues. Fluorescence in situ hybridization localized the genes for ***GPR38*** and GPR39 to separate chromosomes, distinct from the gene encoding the GHS-R and NT-R type 1. The ligand-binding and functional properties of ***GPR38*** and GPR39 remain to be determined.